



IFW

01997.026700

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:)	
	:	Examiner: Not Yet Assigned
Wei LIU et al.)	
	:	Group Art Unit: 1632
Application No.: 10/812,232)	
	:	
Filed: March 29, 2004)	
	:	
For: NOVEL PROTEINS)	
HOMOLOGOUS TO KINASE	:	
SUPPRESSOR OF RAS)	September 13, 2004

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

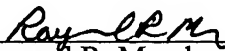
Sir:

In compliance with the duty of disclosure under 37 C.F.R. § 1.56 and in accordance with the practice under 37 C.F.R. §§ 1.97 and 1.98, the Examiner's attention is directed to the documents listed on the enclosed Form PTO-1449. Copies of the listed documents are also enclosed.

It is respectfully requested that the above information be considered by the Examiner and that a copy of the enclosed Form PTO-1449 be returned indicating that such information has been considered.

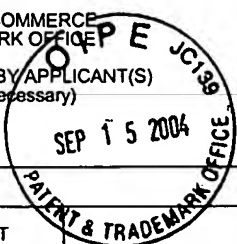
Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our address given below.

Respectfully submitted,



Raymond R. Mandra
Attorney for Applicants
Registration No. 34,382

FITZPATRICK, CELLA, HARPER & SCINTO
30 Rockefeller Plaza
New York, New York 10112-3800
Facsimile: (212) 218-2200

FORM PTO 1449 (modified) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE LIST OF REFERENCES CITED BY APPLICANT(S) (Use several sheets if necessary)			ATTY DOCKET NO. 01997.026700		APPLICATION NO. 10/812,232		
			APPLICANT <p style="text-align: center;">Wei LIU et al.</p>				
			FILING DATE <p style="text-align: center;">March 29, 2004</p>		GROUP		
U.S. PATENT DOCUMENTS							
*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
		6,506,559	01-14-03	Fire et al.	435	6	
FOREIGN PATENT DOCUMENTS							
		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES/NO/ OR ABSTRACT
OTHER DOCUMENT(S) (Including Author, Title, Date, Pertinent Pages, Etc.)							
		Arts, G-J. et al., "Adenoviral Vectors Expressing siRNAs for Discovery and Validation of Gene Function," Genome Res., Vol. 13, pp. 2325-32 (2003).					
		Ballester, A. et al., "Cot Kinase Regulation of IL-2 Production in Jurkat T Cells," J. Immunol., Vol. 159, pp. 1613-18 (1997).					
		Bass, B.L., "RNA Interference. The Short Answer," Nature, Vol. 411, No. 6836, pp. 428-29 (May 2001).					
		Belich, M.P. et al., "TPL-2 Kinase Regulates the Proteolysis of the NF-κB-Inhibitory Protein NF-κB1 p105," Nature, Vol. 397, pp. 363-68 (Jan. 1999).					
		Bockamp, E. et al., "Of Mice and Models: Improved Animal Models for Biomedical Research," Physiol. Genomics, Vol. 11, No. 3, pp. 115-32 (Dec. 2002).					
		Cacace, A.M. et al., "Identification of Constitutive and Ras-Inducible Phosphorylation Sites of KSR: Implications for 14-3-3 Binding, Mitogen-Activated Protein Kinase Binding, and KSR Overexpression," Mol. Cell. Biol., Vol. 19, No. 1, pp. 229-40 (Jan. 1999).					
		Casey, B.P. and Glazer, P.M., "Gene Targeting via Triplex-Helix Formation," Prog. Nucleic Acid Res. Mol. Biol., Vol. 67, pp. 163-92 (2001).					
		Channavajhala, P.L. et al., "Identification of a Novel Human Kinase Supporter of Ras (hKSR-2) That Functions as a Negative Regulator of Cot (Tpl2) Signaling," J. Biol. Chem., Vol. 278, No. 47, pp. 47089-97 (Nov. 2003).					
		Chiariello, M. et al., "Multiple Mitogen-Activated Protein Kinase Signaling Pathways Connect the Cot Oncoprotein to the c-jun Promoter and to Cellular Transformation," Mol. Cell. Biol., Vol. 20, No. 5, pp. 1747-58 (Mar. 2000).					
		Denouel-Galy, A. et al., "Murine Ksr Interacts with MEK and Inhibits Ras-Induced Transformation," Curr. Biol., Vol. 8, pp. 46-55 (1997).					
		Downward, J., "KSR: A Novel Player in the RAS Pathway," Cell, Vol. 83, pp. 831-34 (Dec. 1995).					
		Dumitru, C.D. et al., "TNF-α Induction by LPS is Regulated Posttranscriptionally via a Tpl2/ERK-Dependent Pathway," Cell, Vol. 103, pp. 1071-83 (Dec. 2000).					
EXAMINER				DATE CONSIDERED			

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO 1449 (modified) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE LIST OF REFERENCES CITED BY APPLICANT(S) (Use several sheets if necessary)				ATTY DOCKET NO. 01997.026700		APPLICATION NO. 10/812,232	
				APPLICANT <p style="text-align: center;">Wei LIU et al.</p>			
				FILING DATE <p style="text-align: center;">March 29, 2004</p>		GROUP <p style="text-align: center;">1632</p>	
U.S. PATENT DOCUMENTS							
*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
FOREIGN PATENT DOCUMENTS							
		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES/NO/ OR ABSTRACT
OTHER DOCUMENT(S) (Including Author, Title, Date, Pertinent Pages, Etc.)							
		Elbashir, S.M. et al., "Duplexes of 21-Nucleotide RNAs Mediate RNA Interference in Cultured Mammalian Cells," <i>Nature</i> , Vol. 411, No. 6836, pp. 494-98 (May 2001).					
		Elbashir, S.M. et al., "Functional Anatomy of siRNAs for Mediating Efficient RNAi in Drosophila melanogaster Embryo Lysate," <i>EMBO J.</i> , Vol. 20, No. 23, pp. 6877-88 (Dec. 2001).					
		Eliopoulos, A.G. et al., "Induction of COX-2 by LPS in Macrophages is Regulated by Tpl2-Dependent CREB Activation Signals," <i>EMBO J.</i> , Vol. 21, No. 18, pp. 4831-40 (2002).					
		Galderisi, U. et al., "Antisense Oligonucleotides as Therapeutic Agents," <i>J. Cell. Physiol.</i> , Vol. 181, No. 2, pp. 251-57 (Nov. 1999).					
		Gilks, C.B. et al., "Progression of Interleukin-2 (IL-2)-Dependent Rat T Cell Lymphoma Lines to IL-2-Independent Growth Following Activation of a Gene (Gfi-1) Encoding a Novel Zinc Finger Protein," <i>Mol. Cell. Biol.</i> , Vol. 13, No. 3, pp. 1759-68 (Mar. 1993).					
		Heasman, J., "Morpholino Oligos: Making Sense of Antisense?," <i>Dev. Biol.</i> , Vol. 243, No. 2, pp. 209-14 (Mar. 2002).					
		Holtmann, H. et al., "The MAPK Kinase Kinase TAK1 Plays a Central Role in Coupling the Interleukin-1 Receptor to Both Transcriptional and RNA-Targeted Mechanisms of Gene Regulation," <i>J. Biol. Chem.</i> , Vol. 276, No. 6, pp. 3508-16 (Feb. 2001).					
		Joneson, T. et al., "Kinase Suppressor of Ras Inhibits the Activation of Extracellular Ligand-Regulated (ERK) Mitogen-Activated Protein (MAP) Kinase by Growth Factors, Activated Ras, and Ras Effectors," <i>J. Biol. Chem.</i> , Vol. 273, No. 13, pp. 7743-48 (Mar. 1998).					
		Kane, L.P. et al., "Akt-Dependent Phosphorylation Specifically Regulates Cot Induction of NF-κB-Dependent Transcription," <i>Mol. Cell. Biol.</i> , Vol. 22, No. 16, pp. 5962-74 (Aug. 2002).					
		Knauert, M.P. and Glazer, P.M., "Triplex Forming Oligonucleotides: Sequence-Specific Tools for Gene Targeting," <i>Hum. Mol. Gen.</i> , Vol. 10, No. 20, pp. 2243-51 (2001).					
		Kornfeld, K. et al., "The ksr-1 Gene Encodes a Novel Protein Kinase Involved in Ras-Mediated Signaling in <i>C. elegans</i> ," <i>Cell</i> , Vol. 83, pp. 903-13 (Dec. 1995).					
		Lin, X. et al., "The Proto-Oncogene Cot Kinase Participates in CD3/CD28 Induction of NF-κB Acting through the NF-κB-Inducing Kinase and IκB Kinases," <i>Immunity</i> , Vol. 10, pp. 271-80 (Feb. 1999).					
		Michaud, N.R. et al., "KSR stimulates Raf-1 Activity in a Kinase-Independent Manner," <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 94, pp. 12792-96 (Nov. 1997).					
EXAMINER				DATE CONSIDERED			

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO 1449 (modified) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE LIST OF REFERENCES CITED BY APPLICANT(S) (Use several sheets if necessary)				ATTY DOCKET NO. 01997.026700		APPLICATION NO. 10/812,232	
				APPLICANT <p style="text-align: center;">Wei LIU et al.</p>			
				FILING DATE <p style="text-align: center;">March 29, 2004</p>		GROUP <p style="text-align: center;">1632</p>	
U.S. PATENT DOCUMENTS							
*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
FOREIGN PATENT DOCUMENTS							
		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES/NO/ OR ABSTRACT
OTHER DOCUMENT(S) (Including Author, Title, Date, Pertinent Pages, Etc.)							
		Micklefield, J., "Backbone Modification of Nucleic Acids: Synthesis, Structure and Therapeutic Applications," Curr. Med. Chem., Vol. 8, No. 10, pp. 1157-79 (Aug. 2001).					
		Miyoshi, J. et al., "Structure and Transforming Potential of the Human cot Oncogene Encoding a Putative Protein Kinase," Mol. Cell. Biol., Vol. 11, No. 8, pp. 4088-96 (Aug. 1991).					
		Morrison, D., "KSR: a MAPK Scaffold of the Ras Pathway?," J. Cell Sci., Vol. 114, No. 9, pp. 1609-12 (2001).					
		Müller, J. et al., "C-TAK1 Regulates Ras Signaling by Phosphorylating the MAPK Scaffold, KSR1," Mol. Cell, Vol. 8, pp. 983-93 (Nov. 2001).					
		Müller, J. et al., "Identification of B-KSR1, a Novel Brain-Specific Isoform of KSR1 that Functions in Neuronal Signaling," Mol. Cell. Biol., Vol. 20, No. 15, pp. 5529-39 (Aug. 2000).					
		Neff, L. et al., "NF-κB and the MAP Kinases/AP-1 Pathways are Both Involved in Interleukin-6 and Interleukin-8 Expression in Fibroblast-Like Synoviocytes Stimulated by Protein I/II, a Modulin from Oral Streptococci," Cell. Microbiol., Vol. 3, No. 10, pp. 703-12 (2001).					
		Nguyen, A. et al., "Kinase Suppressor of Ras (KSR) is a Scaffold Which Facilitates Mitogen-Activated Protein Kinase Activation In Vivo," Mol. Cell. Biol., Vol. 22, No. 9, pp.3035-45 (May 2002).					
		O'Mahony, A. et al., "Activation of the Heterodimeric IκB Kinase α (IKKα)-IKKβ Complex is Directional: IKKα Regulates IKKβ Under Both Basal and Stimulated Conditions," Mol. Cell. Biol., Vol. 20, No. 4, pp. 1170-78 (Feb. 2000).					
		O'Neil, N.J. et al., "RNA-Mediated Interference as a Tool for Identifying Drug Targets," Am. J. Pharmacogenomics, Vol. 1, No. 1, pp. 45-53 (2001).					
		Paddison, P.J. et al., "Stable Suppression of Gene Expression by RNAi in Mammalian Cells," Proc. Natl. Acad. Sci. USA, Vol. 99, No. 3, pp. 1443-48 (Feb. 2002).					
		Reynolds, A. et al., "Rational siRNA Design for RNA Interference," Nat. Biotechnol., Vol. 22, No. 3, pp. 326-30 (Mar. 2004).					
		Roy, F. et al., "KSR is a Scaffold Required for Activation of the ERK/MAPK Module," Genes Dev., Vol. 16, pp. 427-38 (2002).					
		Salmerón, A. et al., "Direct Phosphorylation of NF-κB1 p105 by the IκB Kinase Complex on Serine 927 is Essential for Signal-Induced p105 Proteolysis," J. Biol. Chem., Vol. 276, No. 25 pp. 22215-22 (June 2001).					
EXAMINER				DATE CONSIDERED			

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO 1449 (modified) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE LIST OF REFERENCES CITED BY APPLICANT(S) (Use several sheets if necessary)				ATTY DOCKET NO. 01997.026700		APPLICATION NO. 10/812,232	
				APPLICANT Wei LIU et al.			
				FILING DATE March 29, 2004		GROUP 1632	
U.S. PATENT DOCUMENTS							
*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
FOREIGN PATENT DOCUMENTS							
		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES/NO/ OR ABSTRACT
OTHER DOCUMENT(S) (Including Author, Title, Date, Pertinent Pages, Etc.)							
		Sasal, H. et al., "Syrian Hamster Embryo Cell Lines Useful for Detecting Transforming Genes in Mouse Tumours: Detection of Transforming Genes in X-Ray-Related Mouse Tumours," Br. J. Cancer, Vol. 67, pp. 262-67 (1993).					
		Schlesinger, T.K. et al., "The TAO of MEKK," Front. Biosci., Vol. 3, pp. D1181-86 (Nov. 1998).					
		Sioud, M., "Nucleic Acid Enzymes as a Novel Generation of Anti-Gene Agents," Curr. Mol. Med., Vol. 1, No. 5, pp. 575-88 (Nov. 2001).					
		Song, E. et al., "RNA Interference Targeting Fas Protects Mice from Fulminant Hepatitis," Nat. Med., Vol. 9, No. 3, pp. 347-51 (Mar. 2003).					
		Stewart, S. et al., "Kinase Suppressor of Ras Forms a Multiprotein Signaling Complex and Modulates MEK Localization," Mol. Cell Biol., Vol. 19, No. 8, pp. 5523-34 (Aug. 1999).					
		Sugimoto, T. et al., "The Kinase Suppressor of Ras (KSR) Modulates Growth Factor and Ras Signaling by Uncoupling Elk-1 Phosphorylation from MAP Kinase Activation," EMBO J., Vol. 17, No. 6, pp. 1717-27 (1998).					
		Sui, G. et al., "A DNA Vector-Based RNAi Technology to Suppress Gene Expression in Mammalian Cells," Proc. Natl. Acad. Sci. USA, Vol. 99, No. 8, pp. 5515-20 (Apr. 2002).					
		Sundaram, M. and Han, M., "The C. elegans ksr-1 Gene Encodes a Novel Raf-Related Kinase Involved in Ras-Mediated Signal Transduction," Cell, Vol. 83, pp. 889-901 (Dec. 1995).					
		Therrien, M. et al., "KSR, a Novel Protein Kinase Required for RAS Signal Transduction," Cell, Vol. 83, pp. 879-88 (Dec. 1995).					
		Therrien, M. et al., "KSR Modulates Signal Propagation within the MAPK Cascade," Genes Dev., Vol. 10, pp. 2684-95 (1996).					
		Tsatsanis, C. and Spandidos D.A., "The Role of Oncogenic Kinases in Human Cancer," Int. J. Mol. Med., Vol. 5, No. 6, pp. 583-90 (2000).					
		Turek, T.C. et al., "Development and Validation of a Competitive AKT Serine/Threonine Kinase Fluorescence Polarization Assay Using a Product-Specific Anti-Phospho-Serine Antibody," Anal. Biochem., Vol. 299, pp. 45-53 (2001).					
		Wolfer, D.P. et al., "Knockout Mice: Simple Solutions to the Problems of Genetic Background and Flanking Genes," Trends Neurosci., Vol. 25, No. 7, pp. 336-40 (Jul. 2002).					
		Xing, H. et al., "The Protein Kinase KSR Interacts with 14-3-3 Protein and Raf," Curr. Biol., Vol. 7, pp. 294-300 (1997).					
EXAMINER				DATE CONSIDERED			

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO 1449 (<i>modified</i>) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE LIST OF REFERENCES CITED BY APPLICANT(S) (Use several sheets if necessary)				ATTY DOCKET NO. 01997.026700		APPLICATION NO. 10/812,232	
				APPLICANT Wei LIU et al.			
				FILING DATE March 29, 2004		GROUP 1632	
U.S. PATENT DOCUMENTS							
*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
FOREIGN PATENT DOCUMENTS							
		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES/NO/ OR ABSTRACT
OTHER DOCUMENT(S) (Including Author, Title, Date, Pertinent Pages, Etc.)							
		Xing, H.R. et al., "Epidermal Growth Factor Treatment Enhances the Kinase Activity of Kinase Suppressor of Ras," J. Biol. Chem., Vol. 275, No. 23, pp. 17276-80 (June 2000).					
		Xing, H.R. and Kolesnick, R., "Kinase Suppressor of Ras Signals Through Thr²⁶⁹ of c-Raf-1," J. Biol. Chem., Vol. 276, No. 13, pp. 9733-41 (Mar. 2001).					
		Yu, W. et al., "Regulation of the MAP Kinase Pathway by Mammalian Ksr Through Direct Interaction with MEK and ERK," Curr. Biol., Vol. 8, pp. 56-64 (1997).					
		Yu, J-Y. et al., "RNA Interference by Expression of Short-Interfering RNAs and Hairpin RNAs in Mammalian Cells," Proc. Natl. Acad. Sci. USA, Vol. 99, No. 9, pp. 6047-52 (Apr. 2002).					
		Zhang, Y. et al., "Kinase Suppressor of Ras is Ceramide-Activated Protein Kinase," Cell, Vol. 89, pp. 63-72 (Apr. 1997).					
EXAMINER				DATE CONSIDERED			

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Sheet 5 of 5